REMARKS

Indication of Allowable Subject Matter

Applicants greatly appreciate the Examiner's statement in the previous Office Action in which claim 27 has been indicated as allowable. Additionally, Applicants note that claims 8, 10-14, 16-18, 27, and 34-36 are deemed free of the prior art. Because the other objections/rejections of these claims have been overcome by the foregoing amendments to these claims, Applicants respectfully request that at least claims 8, 10-14, 16, 18, and 34-36 are also allowable.

Miscellaneous Issues

The Office Action stated that "[t]his application contains claims 1-7 and 19-23 drawn to an invention nonelected with traverse in Paper No. 17. A complete reply to the final rejection must include a cancellation of nonelected claims or other appropriate action...." *Office Action* at 2. Applicants herein cancel claims 1-7 and 19-23 without prejudice, waiver, or disclaimer.

The Office Action also states the following:

> Newly submitted claims 25-26 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The invention in claims 25-26, a method of protecting a plant by inserting a protein into the plant, is independent and distinct from the elected method, which is a method of protecting a plant by transformation with a nucleic acid. The different methods have different starting materials, different method steps, and different end product.
>
> Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-26 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Office Action at 2. Because claims 25-26 have been withdrawn from consideration, Applicants herein cancel claims 25-26 without prejudice, waiver, or disclaimer.

Objections to Drawings

The drawings have been "objected to for the reasons indicated on the accompanying FORM PTO 948. Corrected drawings are required in reply to the Office Action to avoid abandonment of the application." *Office Action* at 3. As Applicants previously noted in the response submitted October 10, 2002, the FORM PTO 948 again did again not accompany the present Office Action. Even though in the instant Office Action, the Office Action Summary sheet did have Attachment box 2 checked (Notice of Draftsperson's Patent Drawing Review (PTO 948)), the form did not accompany the present Office Action. Accordingly, Applicants respectfully request that the objection to the drawings be held in abeyance until the USPTO sends the objections. Upon receipt of PTO 948, Applicants are willing to amend the drawings to overcome the objections.

Response To Objection To Abstract

The Office Action alleges that:

> The abstract is not description of the instant invention. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The elected claims are drawn to a method of protecting a plant by transformation with a nucleic acid encoding a cystein protease inhibitor. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Office Action at 3. Without admitting to the veracity of the objection, Applicants have replaced the former Abstract with a new Abstract herein. Applicants respectfully request that the objection to the Abstract be withdrawn.

Objections to Sequence Listings

The Office Action states the following:

> This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

> Sequence identifiers are missing from the specification, pg 12, lines 14-17, pg 18, lines 18-20 and 33-34, pg 20, line 3-4, pg 39, lines 13-14, pg 43, lines 13-14, pg 63, line 7, the Brief Description of the Drawings for Figures 1 and 2, and Table 12.

Office Action at 3. As requested by the Examiner, to comply with the applicable Rules, Applicants have now added new sequence listings as SEQ ID NO:5 – SEQ ID NO:17 to reflect the sequence listings in the specification. Additionally, substitute SEQ ID NO:1 – SEQ ID NO:4 are also submitted herewith. Further, the specification has been amended as previously indicated to add the appropriate sequence identifier. Accordingly, Applicants believe that the application now complies with all of the requirements of 37 CFR 1.821-1.825.

Response To Claim Rejections Under 35 U.S.C. §112, First Paragraph

The Office Action states the following:

> Claims 8, 10-14, 17-18 remain rejected and claims 24 and 28-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office Action mailed 10 September [sic, April] 2002, as applied to claims 8-15 and 17-18. Applicant's arguments filed 15 October 2002 have been fully considered but they are not persuasive.
>
> Applicant urges that one of skill in the art would be able to isolate further nucleic acids that encode cysteine protease inhibitors with type I thyroglobulin domains. Applicant cites US Patent 6,312,913, but did not send it (response pg 12).
>
> This is not found persuasive. The specification fails to describe the structural features (*i.e.*, the sequence) of the other nucleic acids that encode such proteins. Applicant's arguments are drawn to enablement, not written description.

Office Action at 4. Applicants respectfully traverse this rejection.

The specification does indeed describe the structural features of further nucleic acids that encode cysteine protease inhibitors containing at least one type I repeated thyroglobulin domain. The nucleic acids are for the sake of briefness indicated as "thyroglobulin genes." The thyroglobulin gene family can be recognized by a number of structural elements of the proteins that are found in the animal kingdom. Specifically, reference is made to SEQ ID NO:2 (FIG. 2)

and the description at pages 18-19, both of which show the consensus sequence. Also, the consensus sequence is shown in FIG. 2 on page 3/13 and in the specification at page 18, line 33-34. Thus, the specification does describe the structural features of the DNA molecules that encode cysteine protease inhibitors with type I repeated thyroglobulin domains. Further, the specification describes the structural features that distinguish proteins with type I repeated thyroglobulin domains that are cysteine protease inhibitors from other proteins with type I repeated thyroglobulin domains.

Claim 16 remains rejected under 35 U.S.C. 112, first paragraph, based on the enablement requirement. Applicants respectfully traverse this rejection. Nevertheless, to advance prosecution, claim 16 has been canceled without prejudice, waiver, or disclaimer. Thus, the rejection of claim 16 has been rendered moot.

The Office Action also states the following:

> Claims 8, 10-14, 17-18 remain rejected and claims 24 and 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting a plant against insect or nematode infestation by transformation with a nucleic acid encoding equistatin, does not reasonably provide enablement for a method of protecting a plant against insect or nematode infestation by transformation for a nucleic acid encoding a cysteine protease inhibitor comprising the type I repeated thyroglobulin domains or encoding a functional fragment of a such a protein or equistatin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Office Action at 6. Applicants respectfully traverse this assertion. One skilled in the art should be able to isolate further thyroglobulin genes in addition to the equstatin gene based on a reading of the specification.

For example, one can use the information of the consensus sequence which is listed in Figure 2:

Thyroglobulin consensus $C(X)_{15-26}P$-C----G-----$QC(X)_{4-10}CWCV$---$G(X)_{14-20}C$

With this sequence, it is possible, based on the absolutely conserved peptide sequence CWCV, to prepare degenerate oligonucleotides. In this sequence, V = valine encoded GTN, where N can be T, C, A, or G; W = tryptophan encoded TGG; and C = cysteine encoded by TGY, where Y can be T or C.

The following table, which could be prepared by one skilled in the art, gives the DNA codons of the amino acids that can be used to identify thyroglobulins.

Amino Acids	SLC	DNA codons
Valine	V	GTT, GTC, GTA, GTG
Cysteine	C	TGT, TGC
Tryptophan	W	TGG

The following is the degenerate nucleic acid code:

AA	CC
GG	TT
UT	M(AC)
R(AG)	W(AT)
S(CG)	Y(CT)
K(GT)	V(ACG)
H(ACT)	D(AGT)
B(CGT)	N(ACGT)

Thus, two degenerate oligonucleotides can be used to isolate genes which contain thyroglobulin domains:

Thyroglobulin Downstream – TGYTGGTGYGTN

Thyroglobulin Upstream – NACRCACCARCA

The primers can be used in a variety of method to isolate full-length genes from either genomic DNA or cDNA. Isolation methods are exemplified by the following Examples A and B.

Example A: A genomic or cDNA library from any organism that is cloned into a cloning vehicle such as plasmid or phage DNA can be used in a PCR reaction that includes a gene-specific primer (Thyroglobulin Downstream or Upstream) and a vector-specific primer. The resulting products can be used as a probe to identify the full-length gene in a situation where the library is plated on filters for example. The hybridizing clones can be purified and sequenced.

Example B: The gene-specific primers Thyroglobulin Up- and Downstream can be used in a RACE PCR reaction to identify cDNA gene products of the 5' and 3' end of the cDNAs. The PCR products can be cloned and sequenced.

The resulting sequenced gene products can be compared to the Thyroglobulin Consensus sequence in order to identify the full gene products as a genuine thyroglobulin. Thus, one skilled in the art is able, based on reading the specification, to isolate further thyroglobulin genes and practice the invention of claims 8, 10-14, 17-18 and 28-39. Applicants respectfully request that the rejection of the claims be withdrawn.

Further, the Office Action states that:

> Claims 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
>
> Neither the instant specification nor the originally filed claims appear to provide support for the phrases "wherein at least one of the proteins... is human p41 invariant chain fragment or a homologue or functional derivative thereof" in claim 37, "wherein at least one of the proteins... is isolated from the sea anemone *Actina equina* and having the amino acid sequences SEQ ID NO:2 or a homologue or functional derivative thereof" in claims 38, and "wherein at least one of the proteins... is a protein isolated from the eggs of chum salmon or a homologue or functional derivative thereof" in claim 39. Thus, such phrases constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrases (*i.e.*, support for the use in the instant method of nucleic acids encoding those proteins) or to cancel the new matter.

Office Action at 7. Applicants respectfully traverse. Nevertheless, to advance prosecution, claims 37-39 have been amended to replace the phrase "wherein at least one of the proteins" with the phrase --wherein the protein--. Support can be found for the amended phrase in the original claims 5-7, and as such the amended claims 37-39 do not include any new matter. Applicants respectfully request that the rejection of claims 37-39 be withdrawn.

Response To Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Office Action states:

> Claims 10-13, 24, 28-33 and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the failing to particularly point out and distinctly claim the subject matter that the Applicant regards as the invention. Dependent claims are included in all rejections. Applicant's arguments filed 15 October 2002 have been fully considered but they are not persuasive.
>
> Applicant urges that the claims have been amended to address the informality issues (response pg 13). This is not found persuasive because the following rejections are new, due to amendments of the claims:
>
> Claim 10 lacks antecedent basis for the limitation "the reproduced plants" in line 4.
>
> Claim 11 lacks antecedent basis for the limitation "the insect or nematode resistant plant" in part (b).
>
> Claims 12 lacks antecedent basis for the limitation "the insect or nematode resistant progeny" in part (a).
>
> In claim 13, the plants and the progeny should be claimed in the alternative.
>
> Claims 28-29 are indefinite in their recitation of "DNA... coding for ... a substantially pure protein." It is unclear what this means. Does it mean the expression vehicle encodes no other protein, even a selection marker?
>
> Claim 30 is indefinite in its recitation of "causing the genome of the cells or tissue to produce a substantially pure polypeptide." A cell or tissue produces many proteins, including many proteins that must be produced simply to make the components of the transcription and translation machinery. It is unclear how a cell or tissue can produce a single protein.
>
> Claims 24, 28-33 and 37-39 are indefinite in their recitation of "functional derivative thereof". The manner in which the derivative is functional is unclear. It is also unclear how the derivative differs from the original protein.
>
> Claims 37-39 are indefinite in their recitation of "homologue". It is unclear how the homologue differs from the original protein.

Office Action at 7-8. Applicants respectfully traverse these rejections, but nevertheless in order to advance prosecution have amended the claims to comply with the Examiner's requests. Applicants believe that the rejections of claims 10-13, 24, 28-33, and 37-39 have been overcome, and respectfully request that the rejections be withdrawn.

Applicants wish to clarify that the foregoing amendments have been made for purposes of better defining the invention in response to the rejections made under 35 U.S.C. § 112, and not in response to the rejections made based on prior art. Indeed, Applicants submit that no substantive

limitations have been added to the claims. Therefore, no prosecution history estoppel arises from these amendments. *Black & Decker, Inc. v. Hoover Svc. Ctr.*, 886 F.2d 1285, 1294 n. 13 (Fed. Cir. 1989); *Andrew Corp. v. Gabriel Elec., Inc.*, 847 F.2d 819 (Fed. Cir. 1988); *Hi-Life Prods. Inc. v. Am. Nat'l Water-Mattress Corp.*, 842 F.2d 323, 325 (Fed. Cir. 1988); *Mannesmann Demag Corp. v. Eng'd. Metal Prods. Co., Inc.*, 793 F.2d 1279, 1284-1285 (Fed. Cir. 1986); *Moeller v. Ionetics, Inc.*, 794 F.2d 653 (Fed. Cir. 1986).

Response To Claim Rejections Under 35 U.S.C. §102

Claims 24, 28-33 and 37-39 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Walsh, *et al.* (WO 92/21753). In particular, the Office Action states:

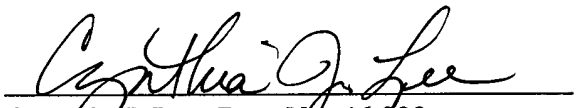
> Applicant urges that the cysteine protease inhibitor of Walsh et al is not of the thyroglobulin family and is not a functional derivative of SEQ ID NO:2 (response pg 14-15).
>
> This is not found persuasive because "functional derivative" is not defined. The protein taught by Walsh et al is a cysteine protease inhibitor, and would thus be a functional derivative of SEQ ID NO:2 or the other claimed cysteine protease inhibitors.

Office Action at 9. Applicants have overcome this rejection because the phrase "functional derivative" has been deleted from the rejected claims, and replaced with the phrase --protein that possesses a biological activity that is substantially similar to the biological activity of the protein having the amino acid sequence SEQ ID NO:2 and which contains at least one type I repeated thyroglobulin domain--. Because the amended feature(s) is not taught or suggested by Walsh *et al.*, Applicants respectfully request that the rejection of the claims based on Walsh *et al.* be withdrawn.

CONCLUSION

In light of the foregoing amendments and for at least the reasons set forth above, Applicant respectfully submits that all objections and/or rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims 8, 10-14, 17-18, 24, 28-39 are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned agent at (770) 933-9500.

Respectfully submitted,



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